

*contd  
a 4*

59. (New) The method of claim 57 wherein said mammal is human.
60. (New) A method of treatment or prophylaxis of a disorder in a mammal comprising administering an effective amount of a compound of claim 29.
61. (New) The method of claim 60 wherein said disorder is an ischaemic disorder of the cardiovascular system.
62. (New) The method of claim 60 wherein said mammal is human.
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Remarks / Explanations

As a result of this preliminary amendment, claims 1-6, 8-16, and 21-62 are pending in the application. Claims 7 and 17-20 have been canceled.

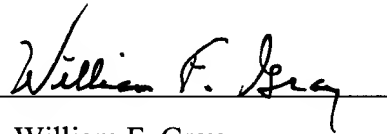
New claim 21 has been broken out of original improper multiple dependent claim 4. New claims 22-24 have been broken out of original improper multiple dependent claim 5. New claims 25-28 have been broken out of original improper multiple dependent claim 6. New claim 29 replaces original claim 7 and reflects the original PCT claim. New claims 30-35 claim material deleted from process claim 8. New claims 36-41 are broken out of original claim 16, drawn to medicaments including the compounds of claims 1-7. New claims 42-62 replace original "use" claims 19 and 20.

No new matter has been added.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned **“Version with markings to show changes made.”**

In view of the above amendments and explanations, this application is deemed to be in condition for allowance, and allowance is accordingly requested.

Respectfully submitted,



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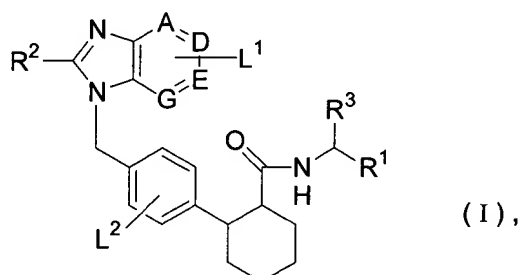
Reg. No. 31018

Phone: (203) 812-2712

Date: 11/25/01

**Version with markings to show changes made:**

1. (Amended) Compounds of the general formula (I)



in which

A, D, E and G are identical or different and represent CH groups or nitrogen atoms,

L<sup>1</sup> and L<sup>2</sup> are identical or different and independently of one another each represents one or more radicals selected from the group consisting of hydrogen, halogen, hydroxyl, carboxyl, cyano, nitro, trifluoromethyl, trifluoromethoxy, (C<sub>1</sub>-C<sub>6</sub>)-alkyl, (C<sub>1</sub>-C<sub>6</sub>)-alkoxy [or] and (C<sub>1</sub>-C<sub>6</sub>)-alkoxycarbonyl,

R<sup>1</sup> represents the CH<sub>2</sub>-OH group, or  
represents a radical of the formula CO-NR<sup>4</sup>R<sup>5</sup>,

in which

R<sup>4</sup> and R<sup>5</sup> are identical or different and each represents hydrogen or  
(C<sub>1</sub>-C<sub>6</sub>)-alkyl,

R<sup>2</sup> represents (C<sub>3</sub>-C<sub>8</sub>)-cycloalkyl,  
represents (C<sub>1</sub>-C<sub>8</sub>)-alkyl which is optionally interrupted by an oxygen or sulphur atom or by a radical NR<sup>6</sup>,

represents a 4- to 8-membered saturated heterocycle which is attached to the imidazole ring via a nitrogen atom and which optionally contains a further oxygen or sulphur atom, or

represents a 4- to 8-membered saturated heterocycle which contains a radical of the formula  $\text{NR}^7$  and optionally additionally one nitrogen, oxygen or sulphur atom,

where  $(\text{C}_3\text{-C}_8)$ -cycloalkyl,  $(\text{C}_1\text{-C}_8)$ -alkyl which is optionally interrupted by an oxygen or sulphur atom, the 4- to 8-membered saturated heterocycle which is attached to the imidazole ring via a nitrogen atom and which optionally contains a further oxygen or sulphur atom and optionally  $(\text{C}_1\text{-C}_8)$ -alkyl which is interrupted by a radical of the formula  $\text{NR}^6$  and optionally the 4- to 8-membered saturated heterocycle which contains a radical  $\text{NR}^7$  and optionally additionally one nitrogen, oxygen or sulfur atom are substituted by one to three hydroxyl groups and/or by a radical of the formula  $-\text{NR}^8\text{R}^9$

in which

$\text{R}^6$  and  $\text{R}^7$  are identical or different and each represents hydrogen,  $(\text{C}_1\text{-C}_6)$ -alkyl, hydroxy- $(\text{C}_1\text{-C}_6)$ -alkyl or  $(\text{C}_3\text{-C}_7)$ -cycloalkyl,

$\text{R}^8$  and  $\text{R}^9$  are identical or different and each represents hydrogen,  $(\text{C}_1\text{-C}_6)$ -alkyl, or  $(\text{C}_3\text{-C}_7)$ -cycloalkyl,

or

$\text{R}^8$  and  $\text{R}^9$  together with the nitrogen atom form a 4- to 8-membered saturated heterocycle which may optionally additionally contain one oxygen or sulphur atom or a radical of the formula  $\text{NR}^{10}$ ,

in which

$R^{10}$  represents hydrogen,  $(C_1-C_6)$ -alkyl or  $(C_3-C_7)$ -cyloalkyl,

and

$R^3$  represents a phenyl, naphthyl, pyrimidinyl, pyridyl, furyl or thienyl ring, where the rings are optionally mono- or polysubstituted by radicals selected from the group consisting of halogen, hydroxyl, carboxyl, cyano, nitro, trifluoromethyl, trifluoromethoxy,  $(C_1-C_6)$ -alkyl,  $(C_1-C_6)$ -alkoxy and  $(C_1-C_6)$ -alkoxycarboxyl,

and their enantiomers and diastereomers and their respective salts, hydrates and[, if appropriate, their] prodrugs.

2. (Amended) Compounds according to Claim 1

where

A, D, E and G each represents the CH group,

or one of the radicals A, D, E and G represents a nitrogen atom and the others each represent the CH group,

$L_1$  and  $L_2$  are identical or different and independently of one another each represents one or more radicals selected from the group consisting of hydrogen, fluorine, chlorine, cyano, trifluoromethyl and trifluoromethoxy,

$R^1$  represents the  $-CH_2-OH$  group, or  
 represents a radical of the formula  $-CO-NR^4R^5$ ,

in which

$R^4$  and  $R^5$  are identical or different and each represents hydrogen or  
 $(C_1-C_3)$ -alkyl,

$R^2$  represents  $(C_3-C_7)$ -cycloalkyl,  
 represents  $(C_1-C_6)$ -alkyl which is optionally interrupted by an oxygen or sulphur  
 atom or by a radical  $NR^6$ ,  
 represents a 5- to 7-membered saturated heterocycle which is attached to the  
 imidazole ring via a nitrogen atom and which optionally contains a further  
 oxygen or sulphur atom, or  
 represents a 5- to 7-membered saturated heterocycle which contains a radical of  
 the formula  $NR^7$  and optionally additionally one nitrogen, oxygen or  
 sulphur atom,

where  $(C_3-C_7)$ -cycloalkyl,  $(C_1-C_6)$ -alkyl which is optionally interrupted by an  
 oxygen or sulphur atom, the 5- to 7-membered saturated heterocycle which is  
 attached to the imidazole ring via a nitrogen atom and which optionally contains  
 one further oxygen or sulphur atom and optionally  $(C_1-C_6)$ -alkyl which is  
 interrupted by a radical  $NR^6$  and optionally the 5- to 7-membered saturated  
 heterocycle which contains a radical of the formula  $NR^7$  and optionally  
 additionally one nitrogen, oxygen or sulphur atom are substituted by one hydroxyl  
 group and/or by a radical of the formula  $-NR^8R^9$ ,

in which

$R^6$  and  $R^7$  are identical or different and each represents hydrogen, (C<sub>1</sub>-C<sub>4</sub>)-alkyl, hydroxy-(C<sub>1</sub>-C<sub>4</sub>)-alkyl or (C<sub>3</sub>-C<sub>6</sub>)-cycloalkyl,

$R^8$  and  $R^9$  are identical or different and each represents hydrogen, (C<sub>1</sub>-C<sub>4</sub>)-alkyl or (C<sub>3</sub>-C<sub>6</sub>)-cycloalkyl,

or

$R^8$  and  $R^9$  together with the nitrogen atom form a 5- to 7-membered saturated heterocycle which may optionally additionally contain one oxygen or sulphur atom or a radical of the formula  $NR^{10}$ ,

in which

$R^{10}$  represents hydrogen, (C<sub>1</sub>-C<sub>4</sub>)-alkyl or (C<sub>3</sub>-C<sub>6</sub>)-cycloalkyl, [.]

and

$R^3$  represents a phenyl, pyridyl or thienyl ring which is optionally mono or polysubstituted by radicals selected from the group consisting of fluorine, chlorine, cyano, trifluoromethyl and trifluoromethoxy,

and their enantiomers and diastereomers and their respective salts, hydrates and[, if appropriate, their] prodrugs.

3. (Amended) Compounds according to Claim 1 or 2

where

A, D and E each represent the CH group,

G represents a nitrogen atom or represents the CH group,

L<sup>1</sup> and L<sup>2</sup> each represent hydrogen,

R<sup>1</sup> represents a radical of the formula -CO-NR<sup>4</sup>R<sup>5</sup>,

in which

R<sup>4</sup> and R<sup>5</sup> each represent hydrogen,

R<sup>2</sup> represents (C<sub>1</sub>-C<sub>4</sub>)-alkyl which is optionally interrupted by an oxygen atom, or represents a 4-R<sup>7</sup>-piperazin-1-yl radical,

where (C<sub>1</sub>-C<sub>4</sub>)-alkyl, which is optionally interrupted by an oxygen atom, is substituted by a hydroxyl group or by a radical of the formula -NR<sup>8</sup>R<sup>9</sup>,

in which

R<sup>7</sup> represents hydrogen, (C<sub>1</sub>-C<sub>4</sub>)-alkyl or (C<sub>3</sub>-C<sub>6</sub>)-cycloalkyl,

R<sup>8</sup> and R<sup>9</sup> are identical or different and each represents hydrogen, (C<sub>1</sub>-C<sub>4</sub>)-alkyl or (C<sub>3</sub>-C<sub>6</sub>)-cycloalkyl,

or

R<sup>8</sup> and R<sup>9</sup> together with the nitrogen atom form a morpholine radical,



and

$R^3$  represents a phenyl or pyridyl radical which may optionally be mono- or polysubstituted by fluorine,

and their enantiomers and diastereomers and their respective salts, hydrates and[, if appropriate, their] prodrugs.

4. (Amended) Compounds according to [any of] Claim[s] 1[ to 3]

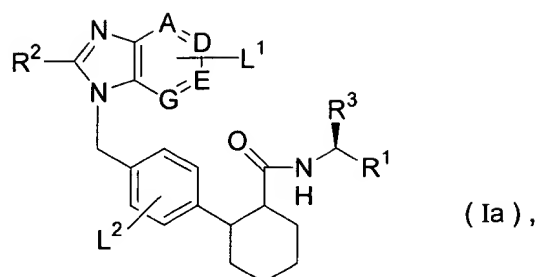
where

the radical  $R^1$  represents a radical of the formula  $CO-NR^4R^5$  where  $R^4$  and  $R^5$  are [as defined above] hydrogen.

and

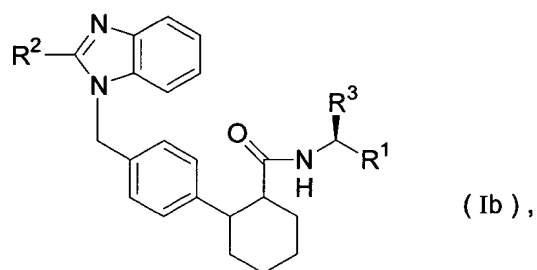
the other radicals are as defined in Claim[s] 1 [to 3].

5. (Amended) Compounds according to [any of] Claim[s] 1 [to 4], characterized by the following stereochemistry according to formula (Ia):



where the substituents  $R^1$ ,  $R^2$ ,  $R^3$ ,  $L^1$  and  $L^2$  and the radicals A, D, E and G are each as defined in Claim[s] 1 [to 4].

6. (Amended) Compounds according to [any of] Claim[s] [1 to 5], having structural formula Ib and characterized by the following stereochemistry according to formula (Ib)



in which

$R^1$  represents a group  $-C(O)-NH_2$ ,

$R^2$  represents  $(C_1-C_4)$ -alkyl which is substituted at the terminal C atom by a hydroxyl group,

$R^3$  represents a phenyl ring which is optionally substituted in the para position by fluorine,

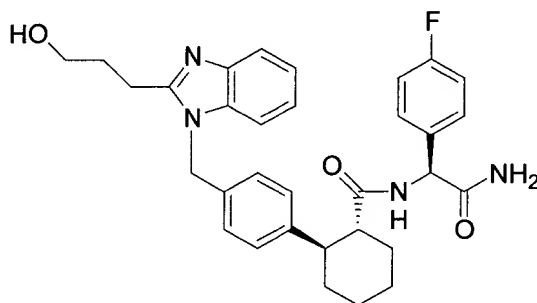
or

represents a pyridyl radical,

and their diastereomers and their respective salts, hydrates and[, if appropriate, their] prodrugs.

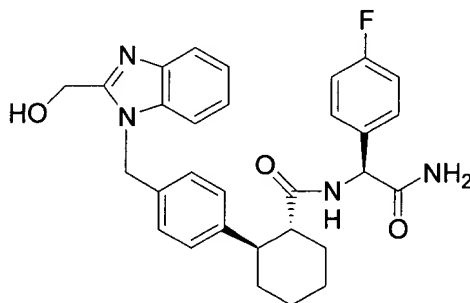
7. (Canceled) Compounds of the general formula (I) of the following structures:

(S)-N-{[(1*R*,2*R*)-2-{4-{[2-(3-hydroxypropyl)-1*H*-benzimidazol-1-yl]methyl}-phenyl}-cyclohex-1-yl]carbonyl}-(4-fluorophenyl)glycinamide:



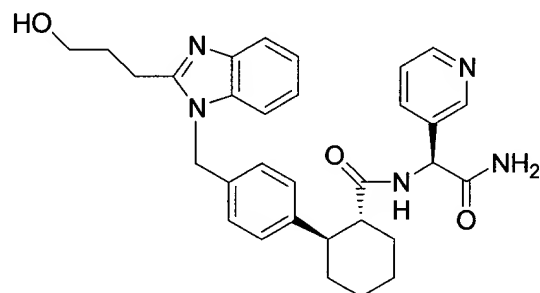
and their salts, hydrates and, if appropriate, their prodrugs.

(S)-N-{[(1*R*,2*R*)-2-{4-{[2-hydroxymethyl)-1*H*-benzimidazol-1-yl]methyl}-phenyl}-cyclohex-1-yl]carbonyl}-(4-fluorophenyl)glycinamide:

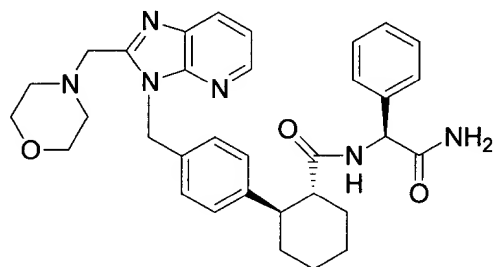


(S)-N-{[(1*R*,2*R*)-2-{4-{[2-(2-hydroxyethyl)-1*H*-benzimidazol-1-yl]methyl}-phenyl}-cyclohex-1-yl]carbonyl}-phenylglycinamide:

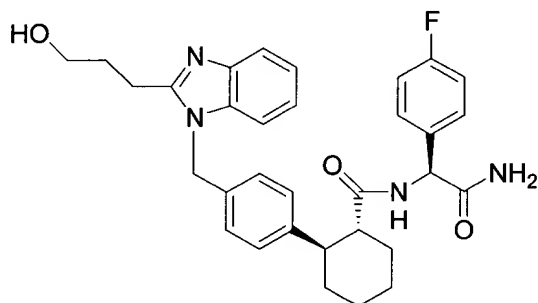
(S)-N-{[(1*R*,2*R*)-2-{4-{[2-(3-hydroxypropyl)-1*H*-benzimidazol-1-yl]methyl}-phenyl}-cyclohex-1-yl]carbonyl}-(3-pyridyl)glycinamide:



(S)-N-{{{(1*R*,2*R*)-4-{2-[2-morpholin-4-yl-methyl]-1*H*-pyrido[2,3-*d*]imidazol-1-yl]methyl}-phenyl}-cyclohex-1-yl]carbonyl}-phenylglycinamide:

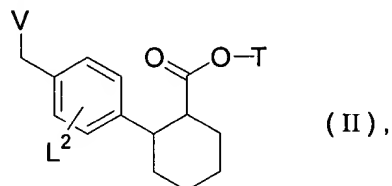


(S)-N-{[(1*R*,2*R*)-2-{4-{[2-(3-hydroxypropyl)-1*H*-benzimidazol-1-yl]methyl}-phenyl}-cyclohex-1-yl]carbonyl}-(4-fluorophenyl) glycinamide:



8. (Amended) Process for preparing compounds of the general formula (I) according to Claim[s] 1 [to 7], characterized in that

[[A]] (A) compounds of the general formula (II)



in which

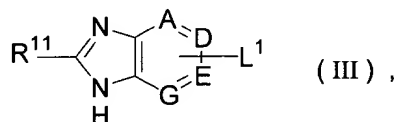
$L^2$  is as defined above in claim 1,

T represents (C<sub>1</sub>-C<sub>4</sub>)-alkyl, [preferably methyl or tert-butyl,]

and

V represents a suitable leaving group, [such as, for example, halogen, meslyate or tosylate, preferably bromine,]

are initially converted by reaction with compounds of the general formula (III)



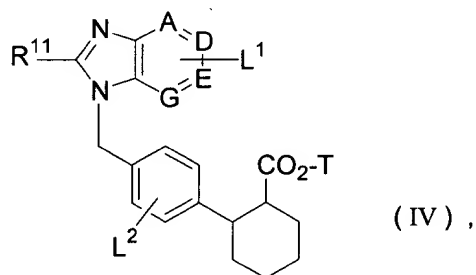
in which

A, D, E, G, and  $L^1$  are each as defined above in claim 1

and

$R^{11}$  has the meaning of  $R^2$  given above in claim 1, where amino and hydroxyl functions are optionally blocked by suitable amino- or hydroxyl- protective groups,

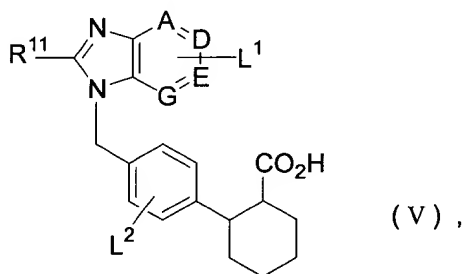
in inert solvents, depending on the definition of  $R^{11}$  optionally in the presence of a base, into the compounds of the general formula (IV)



in which

$R^{11}$ , A, D, E, G,  $L^1$ ,  $L^2$  and T are each as defined above in claim 1,

which are converted in a subsequent step using acids or bases into the corresponding carboxylic acids of the general formula (V)

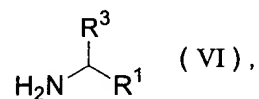


in which

$R^{11}$ , A, D, E, G,  $L^1$ ,  $L^2$  are each as defined above in claim 1,

which are, if appropriate, activated, [in particular] by conversion into a corresponding carboxylic acid derivative, [such as carbonyl halide, carboxylic anhydride or carboxylic ester,]

and which are subsequently reacted [by known methods] with compounds of the general formula (VI) or salts thereof



in which

$\text{R}^1$  and  $\text{R}^3$  are each as defined above in claim 1

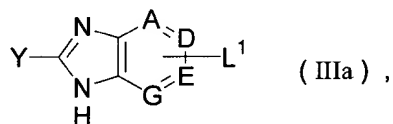
in inert solvents,

and, if  $\text{R}^{11}$  carries one of the abovementioned protective groups, this is optionally removed by customary methods either in the hydrolysis to the acids (IV)  $\rightarrow$  (V) or after the reaction with the compounds of the general formula (VI),

or

[[B]] (B) if  $\text{R}^2$  represents a saturated heterocycle which is attached directly to the imidazole [ringvia] ring via a nitrogen atom,

the above mentioned compounds of the general formula (II) are initially converted with compounds of the general formula (IIIa)



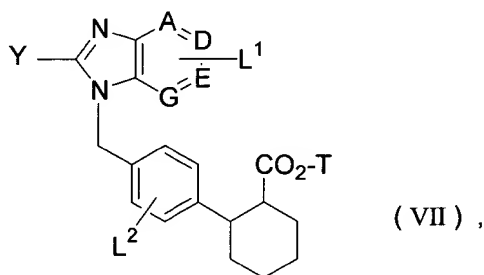
in which

A, D, E, G and L<sup>1</sup> are each as defined above in claim 1

and

Y represents halogen or mesylate, [preferably chlorine, bromine or mesylate,]

in inert solvents into the corresponding compounds of the formula (VII)



in which

Y, A, D, E, G, L<sup>1</sup>, L<sup>2</sup> and T are each as defined above in claim 1,

which are reacted in a subsequent step with compounds of the general formula  
(VIII)

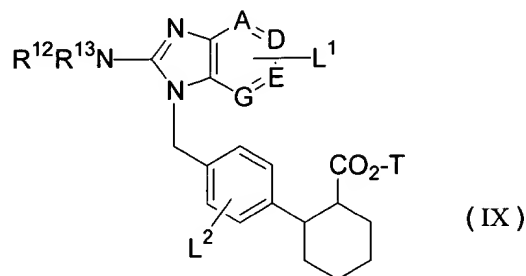


in which

R<sup>12</sup> and R<sup>13</sup> together with the nitrogen atom form a heterocycle according to the definition of R<sup>2</sup> given in claim 1



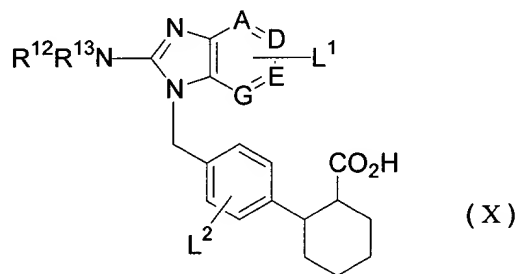
to give compounds of the general formula (IX)



in which

A, D, E, G, L<sup>1</sup>, L<sup>2</sup>, R<sup>12</sup>, R<sup>13</sup> and T are each as defined above in claim 1,

which are, in the subsequent steps, converted as described under [[A]] (A) by hydrolysis into the corresponding carboxylic acids of the general formula (X)



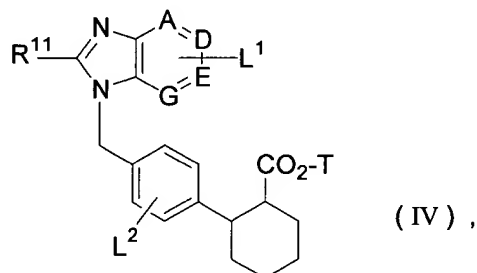
in which

A, D, E, G, L<sup>1</sup>, L<sup>2</sup>, R<sup>12</sup> and R<sup>13</sup> are each as defined above in claim 1

and these compounds are finally reacted with the compounds of the general formula (VI) according to known methods for preparing amides from carboxylic acids and amines and converted into the compounds of the general formula (I)

where the compounds of the general formula (I) obtained according to process variant [[A] or [B]] (A) or (B) can, if appropriate, subsequently be converted into the corresponding salts [by reaction with, for example, an acid].

9. (Amended) Compounds of the general formula (IV)

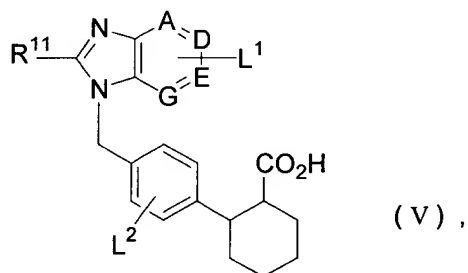


in which

A, D, E, G, L<sup>1</sup>, L<sup>2</sup>, R<sup>11</sup> and T are each as defined above in claim 1,

and their enantiomers and diastereomers and their respective salts.

10. (Amended) Compounds of the general formula (V)

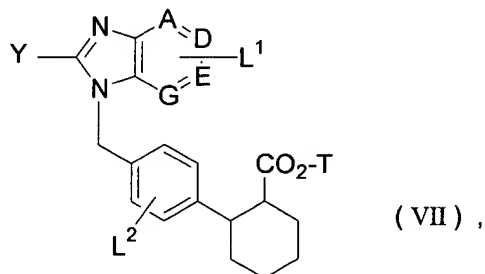


in which

A, D, E, G, L<sup>1</sup>, L<sup>2</sup> and R<sup>11</sup> are each as defined above in claim 1,

and their enantiomers and diastereomers and their respective salts.

11. (Amended) Compounds of the general formula (VII)

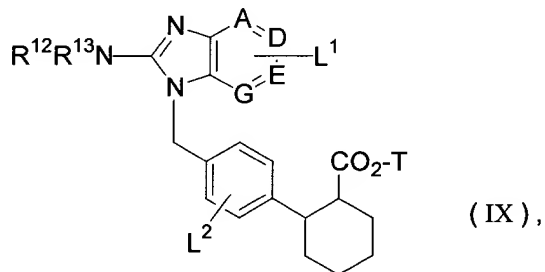


in which

A, D, E, G, L<sup>1</sup>, L<sup>2</sup>, Y and T are each as defined above in claim 1,

and their enantiomers and diastereomers and their respective salts.

12. (Amended) Compounds of the general formula (IX)

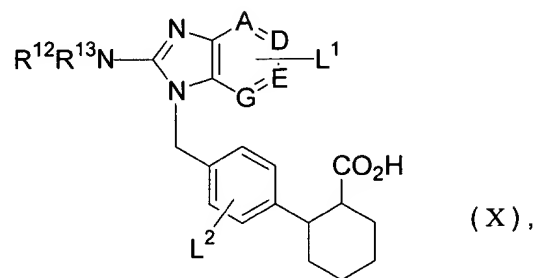


in which

A, D, E, G, L<sup>1</sup>, L<sup>2</sup>, R<sup>12</sup>, R<sup>13</sup> and T are each as defined above in claim 1,

and their enantiomers and diastereomers and their respective salts.

13. ( Amended) Compounds of the general formula (X)



in which

A, D, E, G, L<sup>1</sup>, L<sup>2</sup>, R<sup>13</sup>, R<sup>12</sup> are each as defined above in claim 1.

and their enantiomers and diastereomers and their respective salts.

16. (Amended) [Medicaments], A pharmaceutical composition comprising a compound of the general formula (I) according to [any of] Claim[s] 1 [to 7] in admixture with at least one pharmaceutically acceptable, essentially non-toxic carrier or excipient.
17. (Canceled) Compounds according to any of claims 1 to 7 for the prophylaxis and/or treatment of disorders in humans and animals.
18. (Canceled) Compounds according to any of Claims 1 to 7 for preparing medicaments for the prophylaxis and/or treatment of disorders in humans and animals.
19. (Canceled) Use of compounds according to any of Claims 1 to 7 for preparing medicaments for the prophylaxis and/or treatment of disorders in humans and animals.

20. (Canceled) Use of compounds according to any of Claims 1 to 7 for preparing medicaments for the treatment and/or prophylaxis of ischaemic disorders of the cardiovascular system.